



EXPRESS MAIL NO. ED328068567

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: : M. Bahramian and H. Zarbl
Application No. : 09/472,558
Filed: : December 27, 1999
For : *MUTING GENE ACTIVITY
USING A TRANSGENIC NUCLEIC ACID*

Examiner : Peter Paras, Jr.
Art Unit: : 1632
Docket No. : 9.001
Customer # : 46167

Mail Stop RCE
Commissioner for Patents
P.O. Box 1450
Washington DC 20231-1450

DECLARATION UNDER 37 CFR 1.131

Honorable Commissioner:

- [1] We are Mohammad B. Bahramian and Helmut Zarbl, co-inventors of the subject matter of the rejected claims of the above-identified patent application.
- [2] The attached reproductions of pages of our notebooks contain entries of details of experiments that are described in the patent application, as follows.
- [3] Results on pages 195-197 and interpretations on pages 198-199 correspond to measurement of RNA harvested approximately 24 hours post-electroporation. The samples are analyzed on a long sequencing gel and the data for this Experiment #1 is shown as Fig. 2A in the patent application.
- [4] The RNA used for Experiments #2 and #3 are the same, but different than Experiment #1, harvested 24 hours after electroporation and used different probes synthesized on different days.
- [5] The Experiment #2 starts on page 179, continues on page 183 and finishes on page 185. The data for Experiment #3 (RNA 1 with probe 2) are recorded on pages 186-188.

[6] The results of Experiments #2 and #3 are consistent with the first 24 hour measurement of Experiment #1 shown in Fig. 2A.

[7] A 48-hour measurement experiment starts on page 200 of the notebook and continues through page 202 plus a Phosphorimage insert between pages 202 and 203. The result of this experiment is shown as Fig. 2B in the patent application.

[8] Pages 205-235 show results of experiments showing that partial gene muting can be effected by partial sequences of the procollagen gene.

[9] Specifically, pages 205-224 show that a dsDNA fragment containing 220 bp of the gene promoter plus 115 bp of exon-1 of the gene are sufficient to cause transcriptional suppression of the target gene. The results of this experiment are shown in Fig. 3, 4 and 5 of the patent application.

[10] Further, pages 225-235 describe other experiments demonstrating muting effect of partial sequences from the collagen gene including fragments containing (a) the basal promoter (transcription-start-proximal 222 bp sequences) and exons 1-5 and introns 1-4; and (b) the basal promoter, exon-1 and 390 bp of exon-1 proximal intron-1. The results of these experiments are shown in Fig. 6A of the patent application.

[11] These results were produced in the United States.

[12] These results of these experiments are those described in Examples 1-7, 9 and 10 of the patent application. These results include a reduction to practice of the subject matter of the rejected claims of the patent application.

[13] These results were obtained before December 23, 1997, the effective filing date of Fire et al. US PN 6,506,559 and were submitted in the instant patent application before January 14, 2003, the publication date of Fire et al.'s patent.

[14] All statements made of our own respective knowledge are true and all statements made on information and belief we respectively believe are true.

[15] We have been warned that willful false statements and the like are punishable by up to \$10,000 fine or up to five years imprisonment, or both, and may jeopardize the validity of the instant patent application or any patent issuing from it.



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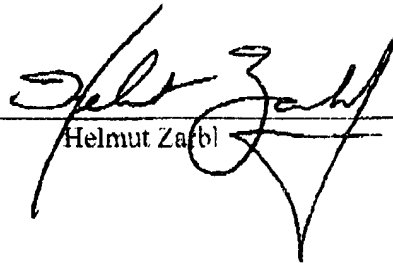
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[14] All statements made of our own respective knowledge are true and all statements made on information and belief we respectively believe are true.

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